NEUROFEEDBACK AND CHRONIC PAIN

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Acknowledgment
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Overview

- National Institute of Neurological Disorders and Stroke of the National Institutes of Health
  - "What is Chronic Pain?
  - While acute pain is a normal sensation triggered in the nervous system to alert you to possible injury and the need to take care of yourself, chronic pain is different. Chronic pain persists. Pain signals keep firing in the nervous system for weeks, months, even years. There may have been an initial mishap – sprained back, serious infection, or there may be an ongoing cause of pain – arthritis, cancer, ear infection, but some people suffer chronic pain in the absence of any past injury or evidence of body damage… “
  - www.ninds.nih.gov/disorders/chronic_pain.htm

Overview

- Fifteen to 20 percent of adults worldwide suffer from persistent, or chronic, pain. Half the primary care patients who develop a chronic pain condition fail to recover within a year - WHO.

Chronic Pain: Cortical Basis
Chronic Pain

- Neurophysiology of Pain: History
  - Early 20th Century: Pain as simple reflexive response to physical damage
    - Nociception transmitted from peripheral area of damage directly to brain
      - Pain a function of the amount of damage or inflammation of the injured tissue
      - Brain viewed as primarily a passive recipient of sensory information

- Chronic Pain
  - Pain influenced by multiple, interactive neural processes that modulate pain information at many levels, including the cortex
    - Neural adaptation to pain stimuli: repeated exposure to painful stimuli increases one’s sensitivity to stimulation. CNS changes, neural plasticity – the alteration of neural networks. Contributes to chronicity.
  - Gate control theory (Melzack & Wall, 1965)
    - Pain input modulated by spinal cord before reaching the brain
    - Long-term potentiation: long-lasting improvement in communication between two neurons. Stimulation from injured peripheral nerves can lead to a heightened response in the recipient cell, an effect that should enable spinal cord cells to amplify incoming pain signals.
Chronic Pain

- Changes in CNS affects endocrine and immune systems
- Top-down regulation
  - (Fregna, Pascual-Leone & Freedman, 2007)

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Chronic Pain

- Plastic changes in neural networks
  - Neuroplastic processes in corticolimbic structures link the sensory and affective experiences of pain: "limbically augmented pain syndrome"
    - Kindling
    - Exposure to a noxious stimulus (emotional or physical trauma) results in a sensitized corticolimbic state
    - Amplification, spontaneity, neuroanatomic spreading and cross-sensitization
    - Treatment refractory pain
    - Disturbances of mood, sleep, energy, libido, memory/concentration, behavior, stress tolerance
      - (Rome, HP & Rome, JD, 2001)

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Chronic Pain

- Overlap between depression symptoms and pain, and the amelioration of pain symptoms with anti-depressants
  - (Lindsay & Wyckoff, 1981)
Chronic Pain

- “... pain not only stimulates sensory areas of the brain but also powerfully activates brain areas involved in emotion, such as the anterior cingulate cortex (ACC), a region governing emotional aspects of pain, and the amygdala, which mediates fear and other feelings.”

Chronic Pain

- “body’s pain-control circuit... stretches from the... frontal lobes through underlying brain structures, including the periaqueductal gray, to the spinal cord, where pain-sensitive nerve fibers connect to neurons that transmit pain signals from the rest of the body...cognitive influences on pain operate through this modulatory pathway”

Chronic Pain

  - Hypothesis: the brain bases of social pain are similar to those of physical pain.
  - Participants scanned while playing a virtual ball tossing game in which they were ultimately excluded.
  - Paralleling results from physical pain studies, the anterior cingulate cortex (ACC) was more active during exclusion than during inclusion and correlated positively with self-reported distress.
  - Right ventral prefrontal cortex (RVPFC) was active during exclusion and correlated negatively with self-reported distress.
  - ACC changes mediated RVPFC activity and RVPFC seemed to regulate the distress of social exclusion by disrupting ACC activity.”
Chronic Pain

- Zaza & Baine (2002)
  - 14 studies reported significant association between psychological distress and pain
  - Stress can increase nociception
  - Experiencing distress before pain predicts worse outcomes

Chronic Pain

- Maintenance of chronic pain is facilitated by hypervigilance, appraisal of harm, fear of pain. Roelofs et al, 2002
- Proposed that cortical hyperexcitability may be assoc with increased chronic pain. Zhou 2008

Chronic Pain

- Legrain et al (2011)
  - Pain intensity can be dissociated from the magnitude of responses in the pain matrix. Responses in pain matrix strongly influenced by the context in which the nociceptive stimuli appear - novelty, frequency, randomness, regularity, salience to what one is currently attending to and contrast with background stimulation.
  - Indicates a cortically centered salience/threat detection network.
  - Non-nociceptive stimuli can elicit cortical responses with a spatial configuration similar to that of the pain matrix.
Chronic Pain

  - Reinforcing increased pain reports in response to painful electrical stimulation increases reports of pain intensity and EEG assessed cortical response to pain.

Chronic Pain

- Neuroimaging studies: Role of the brain
- Multiple cortical sites involved
  - Somatosensory cortex sites, insular cortex, anterior cingulate, prefrontal cortex, thalamic nuclei, amygdala
- Brain regions involved in experimentally-induced pain: somatosensory cortex (primary somatosensory cortex, secondary somatosensory cortex) and associative areas, pfc. (Apkarian et al, 2005, Jensen, 2010)
- Areas involved in pain perception in normal, healthy subjects. Sensory info from spinal cord transmitted bilaterally from thalamus to other parts of the brain. Chen (2008); review 1993-2008:

Somatosensory Cortex
**Somatosensory Cortex**

- **S1**: strip behind motor cortex
- **S2**: base of S1 in parietal lobe
- S2 neurons among first to receive nociceptive input
- S1 and S2 encode spatial info (where damage is)
- S2: encoding severity and quality of the stimulus

**Secondary Somatosensory Cortex**

  - SII activity in response to pain related to overall arousal level. Cortex is pre-primed by projections from other cortical and subcortical structures that control the arousal state of the brain. Decreased vigilance attenuates the responsiveness of SII to painful stimuli. SII locates the pain site, explores the magnitude, and compares the hurting to the non-hurting side.

**Insular Cortex**
Insular Cortex

- Insula
  - Deep inside Sylvian fissure near sensory cortex
  - Component of limbic system
  - Encoding sensory information and associated motivation (vs feeling satisfied and physically content)
  - Involved in the affective, aversive aspects of pain. Chen (2008)

ACC, PFC and Social-Emotional Network

- Jensen (2010): Cortical model
  - PFC encodes cognitive aspects of pain
    - Meaning
    - Executive coping decisions
    - More pfc activity, less pain (inhibitory)
    - Top-down influence
  - ACC
    - part of limbic system
    - Top-down influence
    - Related to affective/emotional component (suffering)
    - Motivational-motor aspects
      - Preparing, initiating and following through with coping
      - Fear memory

- ACC, PFC and Social-Emotional Network
Amygdala

PFC

- Catastrophizing (Sullivan et al, 1995)
  - Pain Catastrophizing Scale (PCS) - magnification, rumination, helplessness
  - Catastrophizing correlated with negative affect (depression and anxiety)
  - predictor of adverse pain-related outcomes, (development of persistent pain, enduring pain-related disability, elevated health care costs)
  - Higher levels associated with elevated pain sensitivity in chronic pain patients.
  - associated with reduced pain-anticipatory brain activity - contributed to the hyperalgesic effect of catastrophizing in Fibromyalgia.
  - lateral prefrontal activity mediates the hyperalgesic effect of catastrophizing.
  - The vlPFC and dlPFC (predominantly right lateralized) are involved in emotion regulation and implementation of cognitive strategies that reduce negative emotional experience (reappraisal, changing expectations, beliefs, and judgments about pain).
  - Subjects with greater anticipatory vlPFC activation report less pain in response to uncontrollable noxious stimuli

ACC

- dorsal anterior cingulate cortex (dACC)
  - fMRI feedback (DeCharmes et al, 2005)
  - Standardized Low Resolution Electromagnetic Tomography (sLORETA) (Ozier et al, 2008)
  - Implications for training at FZ or nearby (F1, F2)
  - Cingulate gyrus (ant. & post.) involved in affective and attentional components of pain and response selection. (CZ,CPZ)
PFC

- Placebo induced analgesia
  - Klosterhalfen & Enck (2008) review
    - PFC (increased activity)
    - ACC (decreased activity)
  - PFC may exert executive control over cognitive-evaluative aspects of pain perception. Chen (2008)

Chronic Pain

- Evidence of cortical involvement in the experience and amelioration of pain comes from successful clinical interventions that alter cortical activity
  - fMRI studies (deCharms, et al., 2005): anterior cingulate
  - Direct cortical electrical stimulation of the motor cortex (Nguyen et al., 1999; Nuti et al., 2005)
  - Repeated Transcranial Magnetic Stimulation (rTMS) (Lefaucher et al., 2001; Pleger et al., 2004)
  - Transcranial Direct Current Stimulation (tDCS) (Antal et al., 2001; Nitsche & Paulus, 2001)

EEG and Pain
EEG
- Evidence shows that the experience of pain is linked to EEG activity
- Teaching patients to alter EEG activity to reflect activity that has been shown to be associated with reduced pain may be promising

Alpha
- Alpha is dominant rhythm. Reduced power in sensorimotor or cognitive processes. The lower the alpha power, the more effectively information is transferred through thalamo-cortical and cortico-cortical channels – gating.
- Suppression of alpha rhythm (alpha event-related desynchronization) can "open the gates" to increased pain input from the periphery.
  - Suppression has been seen in primary somatosensory cortex in anticipation of aversive or painful electrical stimulus.
  - The stronger the magnitude of event-related desynchronization of alpha in anticipation of pain, the greater the subjectively rated experience of pain.

Alpha
- When alpha activity increases in anticipation of pain (event-related synchronization - ERS) subjective perception of pain is decreased.
Beta and Alpha

  - Acute and chronic pain; Although intense and painful stimuli increase all EEG frequencies, beta frequencies increase more relative to others and alpha is lower than other frequencies. Recla (2010)
  - Acute pain relief associated with decreases in beta and increases in alpha activity.

Theta

- Chronic pain associated with neurological disorders (e.g. spinal cord injury) show higher amplitude of theta activity in addition to higher amplitudes of beta and lower amplitudes of alpha. Jensen et al (2012)
- Pain meds: same pattern, less severe.
- Candidates for CLT (central lateral thalamotomy)
- Following surgery
- Reduction in pain
- Normalization of EEG patterns

Neurofeedback & Chronic Pain
Neurofeedback & Chronic Pain

- **Neurofeedback studies**
  - Gannon and Sternbach, 1971
    - Patient with three year history of severe headaches following multiple head traumas
    - 32 hours of training alpha in occipital region
    - Increase alpha from 20% to 90% of the time with eyes closed
    - Increase alpha to 50% of the time with eyes open
    - Headaches decreased
    - Able to read for twice as long (30 min) without a headache

- **Neurofeedback & Chronic Pain**
  - Andreychuk and Skriver, 1975
    - 33 migraineurs
    - Three treatments:
      - Handwarming biofeedback
      - Autogenic relaxation instructions
      - Left and right occipital alpha enhancement feedback
    - 10 30-minute sessions
    - Headache reductions in all conditions

- **Neurofeedback & Chronic Pain**
  - Melzack and Perry, 1975
    - 24 patients, multiple chronic pain conditions
    - Including chronic back pain, peripheral nerve injury, pain from cancer
    - Three conditions
      - Self hypnosis and alpha enhancement neurofeedback
      - Self hypnosis alone
      - Alpha enhancement alone
    - Larger increases in alpha output and decreases in pain over the course of treatment for the hypnosis and neurofeedback group
Neurofeedback & Chronic Pain

- Cohen, McArthur and Rickles, 1980
  - 42 migraineurs
  - One of four biofeedback conditions
    - Forehead cooling/handwarming
    - Frontal EEG reduction
    - Temporal artery vasoconstriction
    - Alpha enhancement over right occipital and parietal lobes
  - All reported significant reduction in headaches
  - No significant changes in alpha activity in neurofeedback group

Neurofeedback & Chronic Pain

- Caro and Winter, 2001
  - 15 fibromyalgia patients
  - 40 or more sessions reinforcing 12-15 Hz (SMR or low beta) and inhibiting 4-7 Hz (theta)
  - Significant improvement on a test of attention
  - Strong correlation between improvements in attention and decreases in tender point scores
  - Weak to moderate correlations between attention scores and patient ratings of fatigue

Neurofeedback & Chronic Pain

- Sime, 2004
  - Case report, trigeminal neuralgia
    - 29 neurofeedback and 10 biofeedback sessions
    - Electrode placement and bandwidths varied
    - Temporal lobe and sensory-motor strip electrode placements
    - Consistent inhibits: 2-7 Hz (delta-theta) and 12-30 Hz (high beta)
    - Rewarding 7.5-10.5 Hz activity (low alpha) at T3-T4 – most immediate pain reduction
    - Patient decided to cancel planned surgery (severing trigeminal nerve) and discontinue pain medications
    - Benefits maintained at 13 month follow up
Neurofeedback & Chronic Pain

Jensen et al, 2007
- 18 patients, Complex Regional Pain Syndrome
  - Neurofeedback as part of multidisciplinary pain treatment program
  - Varied protocols, individualized
  - Pain assessed pre and post 30-min neurofeedback session
  - 0-10 pain scale at primary pain site and other sites
  - Other symptoms measured
  - Significant pain reduction reported at primary site
  - Half of participants reported >30% pain reduction
  - Significant improvement in pain at other sites, muscle spasms, muscle tension and global well-being

Neurofeedback & Chronic Pain

Jensen et al (2013)
- 10 patients with SCI pain completed 12 nfb sessions.
- 3 different protocols
  - Central, temporal and parietal locations
  - Enhancing alpha, fast alpha/slow beta
  - Suppressing beta and theta
  - Pre-to post-tx decrease in theta and increase in alpha
- NFB had an immediate effect on pain intensity, post-treatment reduction in worst pain and pain unpleasantness. Improvements maintained at 3 month follow up.

Neurofeedback & Chronic Pain

Kayiran et al (2010)
- Randomized, controlled, rater blind study comparing nfb and SSRI tx of fibromyalgia patients.
  - SMR training at C4.
  - NFB efficacy began at week 2 and reached max. effect at week 4. Max. effect of SSRI reached at week 8.
  - NFB group showed significant decrease in theta/beta ratio.
Neurofeedback & Chronic Pain

- Kayran et al., 2007
  - Case series: 3 patients with fibromyalgia
    - Ten 30-min sessions rewarding SMR and inhibiting theta at C4
    - Each reported decreases in pain
      - On 10 point scale, reductions were 4.0, 1.5 and 3.0
      - One participant showed minimal EEG changes
      - Two participants showed minimal changes in SMR but significant reductions in theta

- Ibric & Dragomirescu (2009)
  - Reviewed 147 cases of chronic pain treated with combinations NFB and biofeedback. Protocols individualized and qEEG assisted.
  - 20 sessions usually necessary to produce positive effects on pain perception and affect.

Neurofeedback & Chronic Pain

- Migraine headaches
  - Stokes & Lapin (2010): combination of EEG neurofeedback and pIR HEG
  - Carmen (2004): pIR HEG
**Case Studies**

**Training Sites**

- **Jensen et al (2009)**
  - O1, O2, P4, CZ, T4, C3, C3-C4, T3-T4, P3-P4, FP1-FP2, FPO2, CZ-FZ, F7-F8, FZ (suggested), F1 & F2 (suggested)

- **Jacobs & Jensen (2015)**
  - CZ, FZ, O2, C4, P4, F4, FP1
  - T3-T4, F3-F4, C3-C4
  - F1 & F2, O1 & O2
Paraplegia Study

- Electrodes located over the primary motor and sensory cortex C4/C3/Cz/P4, one electrode at the time.
- Six out of seven patients reported immediate reduction of pain during neurofeedback training.
- Four patients reported clinically significant long-term reduction of pain (>30%) which lasted at least a month beyond the therapy.
- Best results were achieved with suppressing theta and higher beta (20–30 Hz) power and reinforcing alpha power at C4.

(Hassan, Fraser, Conway, Allan and Vuckovic, 2015)

Assessing Progress

Assessing Progress

Neurofeedback Progress Chart: Matt Fleishman, Ph.D.
Assessing Progress

- Neurofeedback progress chart
- Problem list in client’s words
- 0-4 scale
  - 0 = not at all
  - 1 = just a little
  - 2 = some
  - 3 = pretty much
  - 4 = very much

The Pain Stethoscope

- The pain stethoscope: A clinician’s guide to measuring pain
- Mark P Jensen
  - Professor and Vice Chair for Research, Department of Rehabilitation Medicine, University of Washington School of Medicine, Seattle, WA, USA
  - 2011 Springer Healthcare

Measuring pain intensity

- Pain intensity = magnitude or severity of perceived pain.
- Primary target of pain treatment in the clinical setting
- Rather than asking patients to rate their current pain intensity, clinicians (and patients) are usually interested in treating the patient’s “usual” or average pain.
  - When patients are asked to estimate average pain intensity over a specified period of time patients use different strategies.
  - Some take into account the entire time period - including those times when they experienced no pain.
  - Others might take into account only those times when they felt pain.
  - When patients asked to rate average pain in the past week, they over-estimate by about 10% relative to an average score made up of multiple ratings of current pain obtained over that same week.
  - Not observed for recall ratings of average pain in the past day, however.
### Measuring pain intensity

- The 0-10 Numerical Rating Scale
- The 0-3 Verbal Rating Scale
  - No Pain, Mild Pain, Moderate Pain, Severe Pain
- The 6-Point FACES Pain Scale-Revised

### Measuring pain quality

- Pain Quality Assessment Scale – Revised
  - 20 questions, 0-10 scale
  - Intense, sharp, hot, dull, cold, sensitive, tender, itchy, shooting, numb, electrical, tingling, cramping, radiating, throbbing, aching, heavy, unpleasant, deep, surface, intermittent vs. variable vs. stable
- Leeds Assessment of Neuropathic Symptoms and Signs
  - Neuropathic (nerve damage) vs nociceptive (stimulation of undamaged receptors)
  - Dysesthesia (e.g., “tingling” or “pins and needles”), thermal quality (e.g., “hot” or “burning”), paroxysmal pain (e.g., “electric” or “jumping”), autonomic dysfunction (e.g., “mottled” or “pink” skin), and allodynia (e.g., “sensitive”), hyperalgesia (pain evoked by a pin-prick).

### Measuring pain location

- Pain drawing
Measuring pain behavior

- **PROMIS Pain Behavior Short Form**
  - Patients rate the frequency of each pain behavior listed (when they felt pain) in the past week on a 6-point scale from “Had no pain” or “Never” to “Always.”
  - Irritable, grimaced, moved extremely slowly, moved stiffly, called out for help, isolated self, thrashed
  - Normative scores

Measuring pain interference

- **Assess specific effects of pain on quality of life**
- **Modified Pain Interference Subscale of the Brief Pain Inventory**
  - General activity, mood, walking ability, work, relations, sleep, enjoyment, self-care, recreation, social activities, communication, learning

Measuring sleep quality and depression

- **Medical Outcomes Study Sleep Problem Index**
- **Patient Health Questionnaire-2**
Measuring general physical functioning

- PROMIS Physical Function Short Forms
  - How much difficulty: chores, stairs, walk, run errands

Measuring alcohol and drug use

- Two-item conjoint screen
- Behavioral Risk Factor Surveillance System
- Assessing alcohol use

Measuring global improvement and satisfaction with pain care

- Five-point patient rating of satisfaction with pain management
  - Satisfaction with pain management
  - Satisfaction with specific pain treatment
  - Global impression of change
Conclusions

- Emerging clinical and experimental literature is promising regarding efficacy
- Consistent with neurophysiological literature and learning theory
- Relatively low cost
- Few groups of individuals that would be unsuitable
- Non-invasive
- Minimal side effect risk

Thanks for your attention!